

### **REMARKS**

These remarks are in response to the Office Action dated September 29, 1999. Reconsideration of the application in view of the amendments and following remarks is respectfully requested.

Upon entry of the amendment, claims 1 to 7 will be pending. For the Examiner's convenience, a copy of the claims as they will stand upon entry of the amendments is attached as Exhibit A.

#### **A. Regarding the Amendments**

The Title has been amended to more clearly reflect the subject matter claimed in the subject application. In addition, the specification has been amended to refer to the related application. The amendments merely addresses formalities and do not add new matter. Accordingly, entry of the amendments to the specification respectfully is requested.

Claim 1 has been amended to more clearly indicate that the claimed subject matter is directed to an antibody or an "antigen binding fragment" of an antibody. The amendment is supported, for example, page 14, line 4, through page 15, line 27, generally, and therefore, does not add new matter.

Claim 1 also has been amended to more clearly indicate that the antibody of the invention "is specifically reactive with" an HBGF polypeptide. The amendment is supported, for example, at page 14, lines 4-5, and, therefore, does not add new matter.

In addition, claim 1 has been amended to more clearly indicate that an antibody of the invention, or antigen binding fragment thereof, is specifically reactive with a polypeptide, as characterized, or with an "an antigenic fragment" of such a polypeptide. The amendment is supported, for example, at page 14, lines 9-11, and, therefore, does not add new matter.

Also, claim 1 has been amended to recite that the polypeptide or antigenic fragment has a molecular weight of about 10 kDa to about 20 kDa. The amendment is supported, for example, at page 6, lines 25, through page 7, line 1 and at page 29, lines 18-27.

Furthermore, claim 1 has been amended to recite that the polypeptide or antigenic fragment comprises the amino acid sequence beginning at about amino acid residue 247 from the N-terminus of CTGF, and having mitogenic and chemotactic activity. The amendment is supported, for example, at page 6, lines 25-27, and at page 26, lines 18-19 of TABLE 2, and throughout the Examples, generally.

New claims 4-7 have been added. Claims 4-7 recite various types of antibodies, specifically, a human antibody, a single chain antibody, a humanized antibody, and an antibody fragment. Support for these claims may be found, for example, at page 15, lines 3-23.

In summary, the amendments to the claims are made without prejudice, and only for the purpose of more clearly defining what the Applicants regard as the invention. The above-described amendments are fully supported by the specification and do not add new matter. Accordingly, entry of the amendments to the instant application is respectfully requested.

#### **B. Regarding the Formal Matters**

The Examiner requests that the Title be amended to more clearly reflect the claimed subject matter. The Title has been so amended and, therefore, it is requested that this objection be withdrawn.

The Examiner also requests that the application be amended to refer to related applications. The application has been so amended and, therefore, it is requested that this objection be withdrawn.

**C. Rejection under 35 U.S.C. 112**

The rejection of claims 1 to 3 under 35 U.S.C. 112, second paragraph, as allegedly failing to particularly point out and distinctly claim the subject matter regarded as the invention is respectfully traversed.

The Examiner states that claim 1 is indefinite in that the meaning of the phrase "and which binds with immunoreactive fragments thereof" allegedly is not clear, nor is it clear what the limitation implies beyond that of the first line of the claim. The Examiner also notes that claim 1 contains two periods. Claims 2 and 3 are rejected as depending from an indefinite claim.

Claim 1 has been amended to delete the phrase including "immunoreactive fragments" and to delete a period such that the claim consists of a single sentence. In view of these amendments, it is respectfully requested that the rejection of claims 1 to 3 under 35 U.S.C. 112, second paragraph, be removed.

**D. Prior Art Rejection**

The rejection of claims 1 to 3 under 35 U.S.C. 102(b) as allegedly anticipated by Grotendorst (U.S. Patent No. 5,408,040) is respectfully traversed.

The Examiner interprets the disclosure at page 14 of the instant specification, as an admission that anti-HBGF antibodies of the invention may be reactive with CTGF, and thus are anticipated by the antibodies disclosed and claimed by Grotendorst. The Applicants respectfully disagree with the Examiner.

The standard of anticipation requires that a single prior art reference disclose each and every element of the claimed invention (See, e.g., M.P.E.P. 2131, p.1260). Thus, for a prior patent or other publication to anticipate a claimed invention, a single reference must bear within

its four corners, each and every element of the claimed invention. Grotendorst clearly does not meet this standard of anticipation.

Grotendorst fails to disclose each and every element of the claimed invention. Specifically, Grotendorst teaches an antibody specifically reactive with CTGF, having a molecular weight of about 36-38 kD and having a polypeptide sequence according to SEQ ID NO:2, a 349 amino acid polypeptide. Grotendorst does not distinctly describe or point out that any specific region of CTGF, such as the HBGF fragment as defined in the present invention, is associated with or attributable to any critical characteristics of protein function, such as mitogenic or chemotactic activity. Thus, the teachings of Grotendorst do not define or teach any specific fragment or region of the full length CTGF protein in which applying an antibody would be advantageous.

In addition, Grotendorst does not explicitly describe an antibody that is specific for a polypeptide having the characteristics disclosed in the present invention. As amended, claim 1 of the instant application recites an antibody that is specific for a polypeptide or antigen binding fragment thereof, having a molecular weight of about 10 kD to about 20 kD. Grotendorst does not disclose a polypeptide of this size, but rather, as noted above, discloses a CTGF polypeptide having a molecular weight of about 36-38 kD.

Furthermore, claim 1 as amended, recites an antibody or antigen binding fragment thereof, specific for a polypeptide or antigenic fragment which begins at about amino acid positions 247 or 248 from the N-terminus of CTGF, and has mitogenic and chemotactic activity. <sup>29% of</sup> CTGF  
The antibodies of the present invention specifically react with a specific region or fragment of full length CTGF that is not distinctly disclosed, described or taught by Grotendorst. Until the present invention, no function was attributable to the regions or fragments of CTGF corresponding to HBGF. Rather, Grotendorst teaches antibodies that are specific for a 349 amino acid polypeptide, depicted in SEQ ID NO:2 of its disclosure. Grotendorst provides no

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teaching of applying an antibody beginning at about positions 247 or 248 of the N-terminus of CTGF.

In summary, Grotendorst does not teach each and every element of the present invention. More specifically, Grotendorst does not distinctly describe or disclose antibodies having the characteristics claimed in the present invention. Accordingly, it is respectfully requested that the rejection of claims 1 to 3 under 35 U.S.C. 102(b) be withdrawn. Applicants note that new claims 4 to 7 are also not anticipated by Grotendorst.

In view of the amendments and the above remarks, it is submitted that the claims are in condition for allowance, and notice to that effect is respectfully requested. The Examiner is invited to call Applicants' undersigned representative at (858) 677-1456 if there are any questions relating to this application.

Please charge any additional fees, or make any credits, to Deposit Account No. 07-1895.

Respectfully submitted,

Date: \_\_\_\_\_

1/28/00



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